

Appl. No. 10/529,304
Reply to Official Action mailed on 10/18/2006

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Remarks/Arguments

Claims 1-37 are currently pending in the instant application. Claims 1-37 have been rejected. Claim 29 has been cancelled. Claim 37 has been amended. New claim 38 has been added.

Claim Rejections – 35 USC § 102

Claims 1-6, 8, 11, 12, 14, 17-22, 25-34, 36 and 37 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Spangler (US 6,124,592).

Applicant respectfully traverses the rejection of claim 1 under 35 U.S.C. 102(b). Claim 1 currently of record defines a method of separating ions comprising the steps of:

providing an analyzer region that is operable in both an rf-only mode and in a FAIMS mode;
introducing ions into the analyzer region;
effecting a selective separation of the ions within the analyzer region substantially during operation in the FAIMS mode; and,
extracting the selectively separated ions from the analyzer region substantially during operation in the rf-only mode.

Applicant wishes to draw the Examiner's attention to the final step of claim 1, which recites a step of (emphasis added) "extracting the **selectively separated ions** from the analyzer region substantially **during operation in the rf-only mode.**" As is claimed at claim 1 of the instant application, ions are exposed to **both** the FAIMS mode of operation and the rf-only mode of operation. In particular, at some time after the ions are introduced into the analyzer region the potentials that are applied to electrodes that define the analyzer region are set to values for establishing electric field conditions under which certain ions are retained within the analyzer region, whilst other ions are caused to collide with an electrode (so as to effect a selective separation of the ions). Ions that remain within the

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analyzer region following the FAIMS based separation subsequently are extracted during operation in the rf-only mode. The method as claimed at claim 1 currently of record has the effect of enhancing ion transmission efficiency relative to the prior art methods in which ions are extracted from the analyzer region while the FAIMS mechanism is operative. The reason for this enhancement, as is described in more detail at paragraph [0092] of the application as originally filed, is that ions exiting from between the electrodes of a prior art FAIMS device experience a rapid transition from balanced conditions to unbalanced conditions as a result of the abrupt disappearance of the asymmetric waveform beyond the end of the electrodes. Such ions experience only the dc compensation voltage that is typically applied to one of the electrodes, which causes the ion to be rapidly attracted to such an electrode and collide therewith. By extracting the ions during a mode of operation in which each electrode rod is maintained at a same dc potential relative to every other electrode rod (i.e. rf-only mode), fewer ions suffer collisions with an electrode, and ion transmission efficiency is increased accordingly.

Applicant respectfully submits that Spangler does not teach the invention in as complete detail as is claimed at claim 1 currently of record. In particular, Spangler discloses various ion mobility spectrometer (IMS) and ion mobility storage trap (IMST) designs. Spangler teaches that an oscillating asymmetric potential is superimposed on a dc potential and applied across electrodes of the IMST (col. 8, lines 53-65; col. 12, lines 17-60; col. 14, lines 1-11). That said, Spangler **does not teach nor does he suggest** that an AC (RF) only mode is utilized to **extract** ions from the IMST. In particular, the text appearing at col. 7, lines 43-63 and at col. 23, lines 5-65, does not teach or suggest "extracting the selectively separated ions from the analyzer region substantially during operation in the rf-only mode" as is claimed at claim 1 currently of record. Rather, col. 7 lines 43-63 are found in the "BRIEF DESCRIPTION OF THE DRAWINGS" section, and relate to figures 20A-24B. Figures 20A-24B show simulated ion trajectories for the mesitylene cation in a generic quadrupole ion trap, under various pressure conditions, as discussed in greater detail at col. 19, line 19 through col. 20, line 22. For completeness, Figs. 20A and 20B show the r-direction and z-direction (simulated) trajectories, respectively, for the mesitylene cation at a background gas pressure of 1×10^{-6} mmHg and

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with a symmetric waveform with $V_1 = 1$ volt applied to the ring electrode. Figs. 21A and 21B show the r-direction and z-direction (simulated) trajectories, respectively, for the mesitylene cation at a background gas pressure of 5×10^{-3} mmHg and with a symmetric waveform with $V_1 = 1$ volt applied to the ring electrode. Figs. 22A and 22B show the r-direction and z-direction (simulated) trajectories, respectively, for the mesitylene cation at a background gas pressure of 5×10^{-3} mmHg and with a symmetric waveform with $V_1 = 2$ volts applied to the ring electrode. Figs. 23A and 23B show the r-direction and z-direction (simulated) trajectories, respectively, for the mesitylene cation at a background gas pressure of 5×10^{-3} mmHg and with a symmetric waveform with $V_1 = 8$ volts applied to the ring electrode. At a constant pressure of 5×10^{-3} mmHg the effect of increasing V_1 from 1 volt to 8 volts is that the secular frequency increases from about 29 kilocycles/second in the r-direction and about 63 kilocycles/second in the z-direction to about 250 kilocycles/second in both directions. It is worth noting that Spangler states explicitly at col. 19, lines 59-62 that "further increases in potential lead only to increased amplitudes for the oscillations with no further changes in frequencies. This region of higher pressure, potentials and secular frequencies is the region of interest for the present invention." Stated differently, Figures 20A-23B of the Spangler reference seem to relate only to the behavior of ions within known ion trap mass spectrometers (ITMS), as the pressure, potential and secular frequency values lie outside the region of interest of Spangler's invention. On the other hand, Figures 24A and 24B show the r-direction and z-direction (simulated) trajectories, respectively, for the mesitylene cation at a higher background gas pressure of 200 mmHg and with a symmetric waveform with $V_1 = 1200$ volts applied to the ring electrode. Under these conditions (rf-only), the effect of the background gas is to dampen ion oscillation, such that the mesitylene ion is not deflected in the trap in either the r-direction or the z-direction. Clearly, none of the above-mentioned portions of the Spangler reference teaches "extracting the selectively separated ions from the analyzer region substantially during operation in the rf-only mode," but merely describes ion motion (or lack thereof) within the trap when operated in AC only mode at different background gas pressures, and absent any prior FAIMS separation of the ions.

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Regarding col. 23, line 5-65 of the Spangler reference, Applicant submits that there is no teaching or suggestion of "extracting the selectively separated ions from the analyzer region substantially during operation in the rf-only mode." Spangler merely teaches at lines 17-20 "the endcaps are perforated to allow ... ions to leave the trap through end-cap electrode 2'." Applicant fails to understand how the cited portion of the Spangler reference teaches or suggests "where an AC (RF) only mode is utilized to extract ions from the trap" as the Examiner has asserted at page 2 of the Official Action mailed on 10/18/2006. Although Spangler does state at lines 44-46 "the ions enter trap volume 41 during at least a portion of the AC cycle applied to ring electrode 1," this merely seems to be an acknowledgment by Spangler that during another portion of the AC cycle the ions may not enter the trap. There is no suggestion or teaching that the trap is operating in an rf-only mode. In any event, the cited portion of the Spangler reference seems to discuss only introduction of ions into the trap, and is silent regarding extraction of ions from the trap.

Furthermore, Applicant respectfully submits the "one particular example" appearing at page 2 of the Official Action mailed on 10/18/2006 does not teach or suggest all of the features of claim 1 currently of record, and in particular it does not teach or suggest the final step "extracting the selectively separated ions from the analyzer region substantially during operation in the rf-only mode." In fact, the Examiner has stated:

"The applied asymmetric AC and DC voltages focuses and stores the ions at specific locations within trap volume 41, after which the asymmetric AC potential is removed and an accelerating potential is applied across electrodes 1 and 2, causing the ions to be injected into drift tube 62 for subsequent mobility analysis."

In the above excerpt from page 2 of the Official Action mailed on 10/18/2006, the Examiner seems to be acknowledging that initially the ions are focused and trapped within volume 41 by the application of asymmetric AC and DC potentials, after which the asymmetric AC potential is removed and an accelerating potential is applied. Spangler is silent regarding the nature of the accelerating potential, but he does positively state "the asymmetric AC potential is removed." Spangler does not indicate that the DC potential is removed. Accordingly, this portion of the Spangler reference does not appear to teach or

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suggest extracting ions **during rf-only mode of operation**. Furthermore, although Spangler does state that the amplitude or phase of the AC signal may be modulated during scanning (the ions out of the trap), such AC modulation appears to be **in addition to**, rather than in place of, DC modulation (see col. 14, lines 61-63).

Applicant submits that Spangler does not teach each and every feature of the instant invention in as complete detail as is recited at claim 1 currently of record. Accordingly, claim 1 currently of record is believed to be in proper condition for allowance, and favorable consideration is respectfully requested.

Claim 2 depends directly from believed allowable claim 1 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Having regard to claim 3, Applicant respectfully submits that at col. 10, lines 18-31, Spangler merely teaches an alternative scheme for extracting ions from volume 7. In particular, Spangler states "the high voltage power supply 19 and switches 20 and 21 remove the ions by applying an accelerating potential between the end-cap electrodes." Spangler is silent regarding the nature of the accelerating potential, but certainly he does not teach or suggest that extraction of ions is performed during an rf-only mode of operation, and consequently he does not teach or suggest "controllably switching the analyzer region from the FAIMS mode to the rf-only mode" as is recited at claim 3 currently of record. Accordingly, claim 3 currently of record is also believed to be in proper condition for allowance, and favorable consideration is respectfully requested.

Claim 4 currently of record recites "wherein the analyzer region is provided as a space between a set of parallel rods, the space having first and second ends." Although Spangler does discuss such electrode geometry (see Fig. 5 as well as col. 4, lines 25-61), Spangler does also go on to state at col. 6, lines 23-30 "to date, none of the mass spectrometer devices of FIGS. 5-9 have been successfully used to separate ions at pressure greater than about 10^{-2} mmHg. Any attempt to do so results in loss of signal." At no point does Spangler teach or even suggest the use of the quadrupole rod arrangement (of Fig. 5) as a suitable geometry for use as an IMST. Applicant respectfully submits that Spangler

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does not teach all of the features as claimed at claim 4, and accordingly claim 4 currently of record is believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Having regard to claim 5, Applicant fails to understand the relevance of the statement at item 7 on page 3 of the Official Action mailed on 10/18/2006. How does the alleged teaching of "continuous filling or refilling during the separation and extraction period" properly anticipate the feature as claimed at claim 5, namely "wherein the ions are introduced into the analyzer region substantially during operation of the analyzer region in the rf-only mode?" Claim 5 currently of record does not mention that filling or refilling is continuous, and accordingly the Examiner's argument appears to be irrelevant. Since Spangler fails to teach the feature that is recited at claim 5 currently of record, and since claim 5 depends from believed allowable claim 1, Applicant respectfully submits that claim 5 currently of record is also in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 6 depends indirectly from believed allowable claim 1 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 8 depends indirectly from believed allowable claim 1 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claims 11 and 12 depend from believed allowable claim 1 and are also in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 14 is believed to be in proper condition for allowance for the same reasons that were presented *supra* with reference to claim 4, *mutatis mutandis*. Favorable consideration is respectfully requested.

Claims 17 through 19 depend from believed allowable claim 1 and are also in proper condition for allowance. Favorable consideration is respectfully requested.

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Applicant respectfully traverses the rejection of claim 20 under 35 U.S.C. 102(b).
Claim 20 currently of record defines an apparatus for separating ions comprising:

a set of parallel rods having a space therebetween, the space having first and second ends and defining an analyzer region; and,
an electrical controller for electrically coupling to the set of parallel rods, for applying at least an rf-voltage between the parallel rods of the set of parallel rods in a first operating mode and for applying a combination of an asymmetric waveform voltage and a direct current voltage between the parallel rods of the set of parallel rods in a second operating mode,
wherein, during use, an ion which is being transmitted through the analyzer region is subjected to the first operating mode and to the second operating mode during a period of time the ion is resident within the analyzer region.

Having regard to point 4 on page 3 of the Official Action mailed on 10/18/2006, Applicant respectfully submits that none of the portions of the Spangler reference as identified by the Examiner teaches "a set of parallel rods having a space therebetween, the space having first and second ends and defining an analyzer region." In particular, at col. 5, lines 28-33 Spangler states "when a symmetric RF and DC (optional) potential is applied across the **ring and end-cap electrodes** of the ITMS..." Clearly, a set of parallel rods as claimed at claim 20 currently of record does not include a ring and end-cap electrodes. Col. 9, lines 50-67 and col. 10 lines 1-5 describes the general behaviour of ions under the influence of asymmetric AC and DC potentials, within "a general representation of an ion mobility storage trap" referred to simply as element. The specific geometries that are discussed for element 6 include a structure that is very similar to the 3-D ion trap of mass spectrometry including a ring electrode and two end-cap electrodes, as well as dipolar traps which comprise essentially the top half of the quadrupole trap (i.e. ring electrode and one end-cap). Figure 10A merely shows "element 6" as a box containing volume 7, but is entirely silent regarding the actual electrode geometry of the IMST. Furthermore, as discussed *supra* Spangler does discuss a parallel rod electrode geometry (see Fig. 5 as well as col. 4, lines 25-61) but only in terms of known mass spectrometer (vacuum) devices. Spangler

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goes on to state at col. 6, lines 23-30 "to date, none of the mass spectrometer devices of FIGS. 5-9 have been successfully used to separate ions at pressure greater than about 10^{-2} mmHg. Any attempt to do so results in loss of signal." At no point does Spangler teach the use of the parallel rod arrangement (i.e. of Fig. 5) as a suitable geometry for use as an IMST. Applicant respectfully submits that Spangler does not teach all of the features of the instant invention in as complete detail as is claimed at claim 20, and accordingly claim 20 currently of record is believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claims 21-22 and 25-27 depend either directly or indirectly from believed allowable claim 20 and are also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 28 depends from believed allowable claim 20 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 29 has been cancelled and a new claim 38, which is dependent on claim 37, has been added to the application, as discussed below.

Claims 30 and 31 depend indirectly from believed allowable claim 1 and are also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claims 32 and 33 depend indirectly from believed allowable claim 1 and are also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 36 depends indirectly from believed allowable claim 20 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim 37 has been amended for improved clarity. In particular, the expression "collisionally cooling the selectively separated ions" has been amended to read -- collisionally cooling the selectively separated ions during operation in the rf-only mode --.

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No new matter has been added. Amended claim 37 depends indirectly from believed allowable claim 1 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

New claim 38 has been added to the application. The wording of new claim 38 is substantially the same as that of cancelled claim 29, except new claim 38 depends from amended claim 37. In particular, new claim 38 recites:

“comprising a step prior to the step of extracting the selectively separated ions of: controllably switching the analyzer region from the rf-only mode to the FAIMS mode, so as to effect a selective second separation of the collisionally cooled selectively separated ions.”

New claim 38 depends indirectly from believed allowable claim 1 and is also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claim Rejections – 35 USC § 103

Claims 7, 9, 10, 13, 15, 16, 23, 24 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6, 124,592 to Spangler in view of Whitehouse, U.S. Patent No. 7,034,292.

Claims 7, 9, 10, 13, 15, 16 and 35 depend either directly or indirectly from believed allowable claim 1. Accordingly, claims 7, 9, 10, 13, 15, 16 and 35 are also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

Claims 23 and 24 depend either directly or indirectly from believed allowable claim 20. Accordingly, claims 23 and 24 are also believed to be in proper condition for allowance. Favorable consideration is respectfully requested.

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Applicant looks forward to receiving favourable consideration of the instant application.

Please charge any additional fees required or credit any overpayment to Deposit Account No: 50-1142.

Respectfully submitted,



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